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Improved Enantioselective Synthesis of (−)-Linderol A: Hindered Rotation about Aryl−Csp^3 Bond

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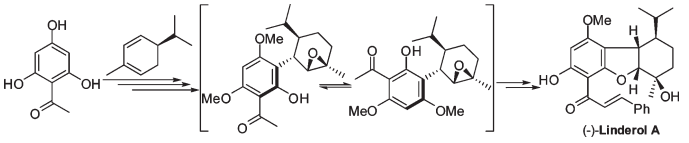

An improved enantioselective total synthesis of (−)-linderol A has been achieved via a five-step reaction with a 21% overall yield, starting from phloroacetophenone and (−)-α-phellandrene, two commercially available reagents. In the diastereoselective epoxidation step, the analysis of the two endocyclic epoxide intermediates reveals a hindered sp^2−sp^3 rotation, which results in rotational diastereoisomers.

Introduction

(−)-Linderol A [(−)-**1**, Figure 1], a monoterpene-substituted chalcone with four asymmetric carbons at the 6 (*R*), 5a (*R*), 9a (*S*), and 9 (*R*) positions, was isolated in 1995 from the fresh bark of *Lindera umbellata* (Lauraceae) by Sashida and co-workers.[1] They also reported the potent inhibitory activity of this natural product on the melanin biosynthesis of B-16 melanoma cells without causing any cytotoxicity on the cultured cells.[1]

Ohta and co-workers were first interested in the total synthesis of **1** because of structural and biological aspects. The first-[2] and second-generation[3] syntheses of (±)-**1** have been previously reported by this group (Scheme 1). In the first-generation synthesis, the critical step of their strategy was a tandem reaction of the 3-ethoxycarbonylcoumarin derivative **2** with dimethylsulfoxonium methylide to give the 2-ethoxycarbonylcyclopenta[*b*]benzofuran-3-ol derivative **3**. The key step of the second-generation synthesis involved a stereoconvergent approach to tetrahydrodibenzofuran derivative **5** from benzo[*b*]cyclobuta[*d*]pyran derivative **4** (Scheme 1).

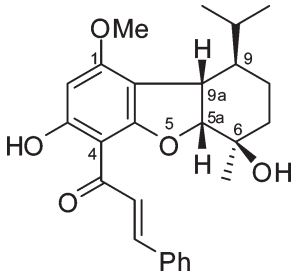

FIGURE 1. Structure of (−)-linderol A [(−)-**1**].

The first synthesis of (−)-**1** and (+)-**1** was achieved via optical resolution of an acetylated intermediate of the total synthesis of (±)-**1** (Scheme 1).[4] Ohta and co-workers have moreover determined the absolute configuration of (−)-**1**, which had not been previously reported by Sashida and co-workers[1] (Figure 1).

Recently, this group has achieved an asymmetric total synthesis of (−)-**1** in 13 steps with 23% overall yield from 5,7-dimethoxycoumarin-3-carboxylic acid using the second-generation strategy.[5] The two key reactions consist in a diastereoselective [2 + 2]

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(2) (a) Yamashita, M.; Ohta, N.; Kawasaki, I.; Ohta, S. *Org. Lett.* **2001**, *3*, 1359–1362. (b) Yamashita, M.; Ohta, N.; Shimizu, T.; Matsumoto, K.; Matuura, Y.; Kawasaki, I.; Tanaka, T.; Maezaki, N.; Ohta, S. *J. Org. Chem.* **2003**, *68*, 1216–1224.

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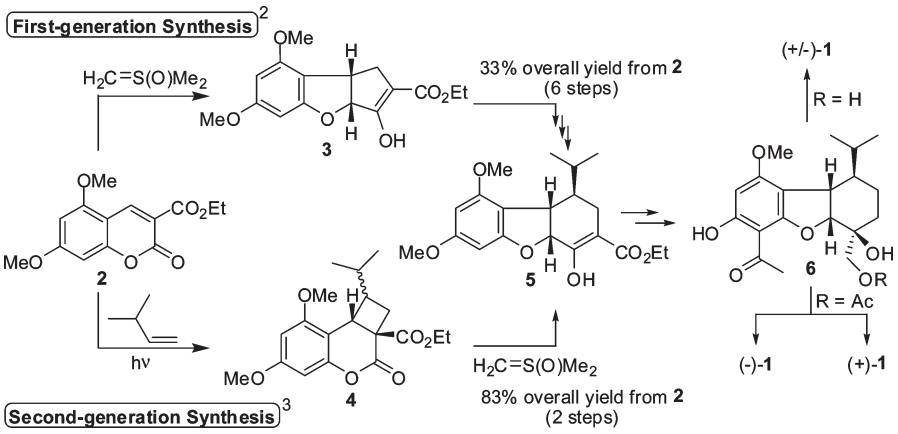
SCHEME 1



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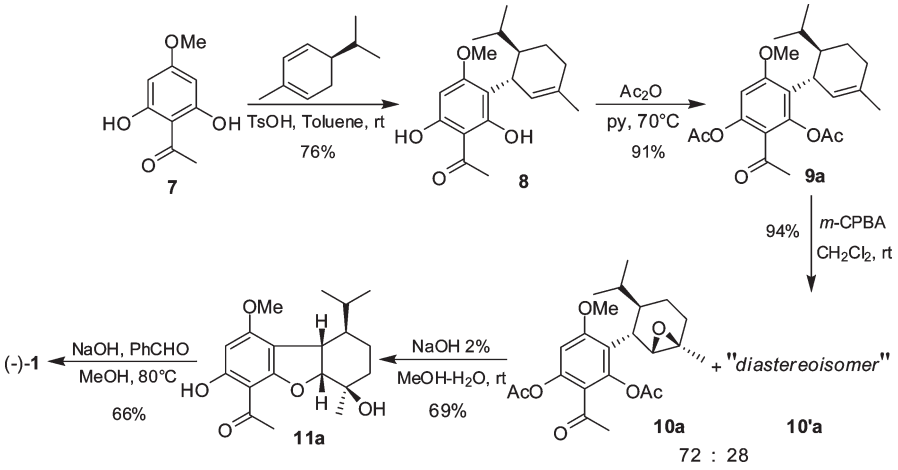

photocycloaddition of a coumarin-3-carboxylate bearing a chiral auxiliary with 3-methyl-1-butene and a subsequent stereoconvergent transformation of the photoadducts with the use of dimethylsulfoxonium methylide to afford a tetrahydrodibenzofuran derivative.

In parallel, we have reported an efficient short enantioselective total synthesis of (−)-**1** via a five-step reaction with a 30% overall yield, starting from 2,6-dihydroxy-4-methoxyacetophenone **7** and (−)-α-phellandrene (Scheme 2).[6]

Two key reactions have been used, terpenylation[7] and a stereospecific intramolecular epoxide opening with a phenolate anion.[8] However, our synthesis presents two shortcomings that are the preparation of the starting reagent 2,6-dihydroxy-4-methoxyacetophenone **7** obtained with poor yields (20%) from the commercially available phloroacetophenone[9] and the low diastereoselectivity of the epoxidation. Indeed, we have reported the formation of a mixture of two supposed diastereomeric epoxides **10a** and **10′a** favoring the desired **10a** in a ratio of 72:28 (evaluated by ^{1}H NMR spectrum). This reaction requires extensive study in order to increase the diastereoselectivity seeing that the epoxide **10a** is the key reagent in the next stereospecific ring closure step; furthermore the structure of the nonproductive epoxide **10′a** was not clearly identified because it was never isolated before.

Herein, we present an improved synthesis of (−)-linderol A after a detailed study of the asymmetric epoxidation.

Results and Discussion

We started our study by reproducing epoxidation of the diacetate compound **9a** with *m*-chloroperoxybenzoic acid. Therefore, the mixture of the two epoxides **10a** and **10′a** was obtained in good yield (Scheme 3). The separation of these two supposed diastereoisomers was attempted by thin-layer chromatography (TLC) and then by column chromatography on silica gel with different solvents. Unfortunately, all our attempts failed (only one spot appeared in TLC plates).

We then decided to carry out epoxidation of the alkene by varying the protecting groups in order to check on the possibility to obtain the mixture of the two epoxides (and the ratio variation). The dibenzoate product **9b** was prepared in good yield (82%) from **8** by the same procedure as for acetylation. Surprisingly, epoxidation of **9b** gave a mixture of the two isomers **10b** and **10′b** with a lower selectivity (60:40).

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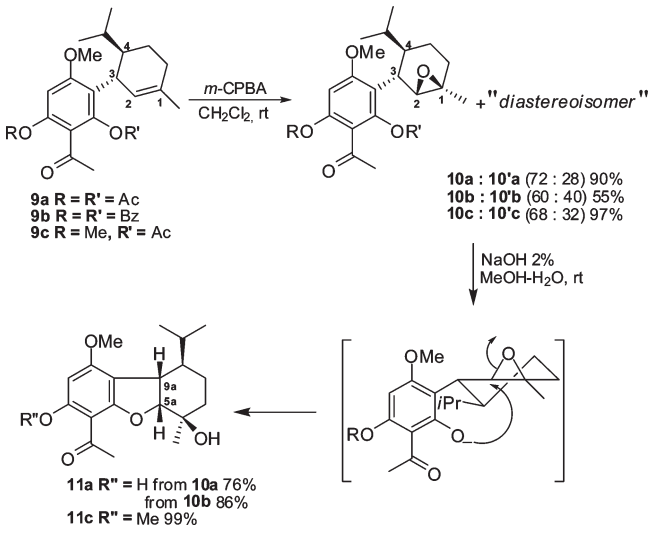
SCHEME 3



With the monoacetate derivative **9c**, epoxidation led to the mixture of the two epoxides **10c** and **10′c** in a ratio of 68:32.

With the mixtures of these inseparable isomers (**10** and **10′**) in hand, we attempted the next ring-closure step via epoxide opening in the presence of 2% sodium hydroxide in methanol−water (1:1). The hexahydrodibenzofuran derivatives **11a**−**c** were obtained with good yields without any byproduct (Scheme 3). The transformation of **10** and **10′** to **11** involves an intramolecular *trans* diaxial cleavage of the epoxide (via a S_N2i mechanism) at its less hindered site, which fixes the stereochemistry of the furan ring at C5a and C9a as *cis*.[8] If the major diastereoisomers (**10a**, **10b**, and **10c**) of the mixtures are considered as the starting material for ring-opening, the exact yield for **11a** and **11c** is over 100% (108%, 143%, and 148%, respectively), which is not a realistic outcome. Thus, we concluded that the mixture of the two epoxides cannot be these diastereoisomers.

Furthermore, the ^{1}H NMR spectra of the mixtures for **10** and **10′** were instructive: it showed similar signals for the C2 proton which appeared as a singlet and for the C3 proton as a doublet with a large coupling constant ($J \approx 11$ Hz) for the two isomers (Table 1). The stereochemistry of this type of endocyclic epoxides has already been studied;[10] it was shown that these two hydrogen atoms (on C2 and C3) are therefore in a *trans* relationship, and it follows that the epoxide ring and the aryl group are also *trans* oriented for the two isomers in each case. Thus, the proposed structure for isomers **10′a**−**c** with the epoxide ring and the aryl moiety in the same face seemed incorrect.

From these results, we hypothesized that atropisomerism was possible around the Car−C3 bond (a sp^2−sp^3 bond) for these compounds (**10**,**10′a**−**c**) (Figure 2). Atropisomerism is usually associated with biaryl systems, where a single bond rotation about the sp^2−sp^2 C−C bond is sufficiently restricted so as to lead to separable conformers.[11] Rotation about the single bond between sp^2- and sp^3-hybridized carbon atoms can also be hindered by bulky substituents.[11] In general, Ar−Csp^3 bonds have very low rotation barriers.[11] Nevertheless, there are some examples of compounds with much higher rotation barriers, such as 9-arylfluorenes, in which case two rotamers may be isolated.[12] Such compounds usually have bulky *ortho*-substituents on the aromatic ring,[13a] or bulky substituents on the benzylic carbon,[13b] or both. A recent study of the bond rotation barriers of 2-aryl perhydropyrrolo[3,4-*c*]pyrrole-1,3-diones where the rigidity of the rings and their substituents retard the C−Ar rotation was also reported.[13c]

TABLE 1. ^{1}H NMR Data of the Mixtures of Endocyclic Epoxides 10 and 10′

	C2-H	C3-H
10a and **10′a**	2.80 (s)	3.06 (d, J = 10.7 Hz)
	2.91 (s)	3.60 (d, J = 10.7 Hz)
10b and **10′b**	2.91 (s)	3.13 (d, J = 10.6 Hz)
	2.91 (s)	3.67 (d, J = 11.6 Hz)
10c and **10′c**	2.78 (s)	3.01 (d, J = 10.6 Hz)
	2.90 (s)	3.53 (d, J = 10.9 Hz)

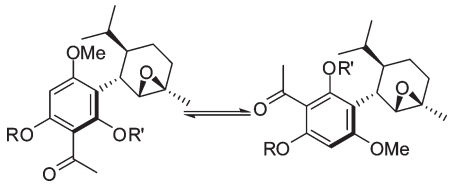


FIGURE 2. Possible structure of rotameric epoxides **10** and **10′**.

To demonstrate the interconversions between **10** and **10′**, compounds **10c** and **10′c** (ratio 68:32) were analyzed by variable-temperature ^{1}H NMR (Figure 3; see the Supporting Information for all spectra). As the temperature increased, the rotation of the pendant aryl ring exchanged the diastereomeric aromatic protons, and the signals broadened and began to coalesce at 370 K with a three-degree uncertainty. We applied the Gutowsky−Holm equation[11a,b] to these signals to obtain a crude estimate of the rate of the Car−C3 bond rotation, and we found $k_c = 28.9\ s^{-1}$. In this case of exchange of the aromatic uncoupled proton between **10c** (major) and **10′c** (minor), two unequally populated sites, we had to estimate two rate constants (see the Supporting Information for more details), which are $k_{\mathbf{10}\rightarrow\mathbf{10'}} = 19.6\ s^{-1}$ and $k_{\mathbf{10'}\rightarrow\mathbf{10}} = 41.7\ s^{-1}$. From these data and the Eyring equation,[11a,b] we calculated $\Delta G^{\ddagger}_{\mathbf{10}\rightarrow\mathbf{10'}} = 82.1 \pm 1\ kJ\cdot mol^{-1}$ and $\Delta G^{\ddagger}_{\mathbf{10'}\rightarrow\mathbf{10}} = 79.8 \pm 1\ kJ\cdot mol^{-1}$. At room temperature (298 K), the rate constants were estimated to be 0.031 and 0.079 s^{-1}, and therefore, half-lives of 32.3 and 12.7 s were deduced. Thus, compounds **10c** and **10′c** are too short-lived to be atropisomers (lower than 1000 s).[11] Nevertheless, these are two relatively long-lived rotamers which should be separable

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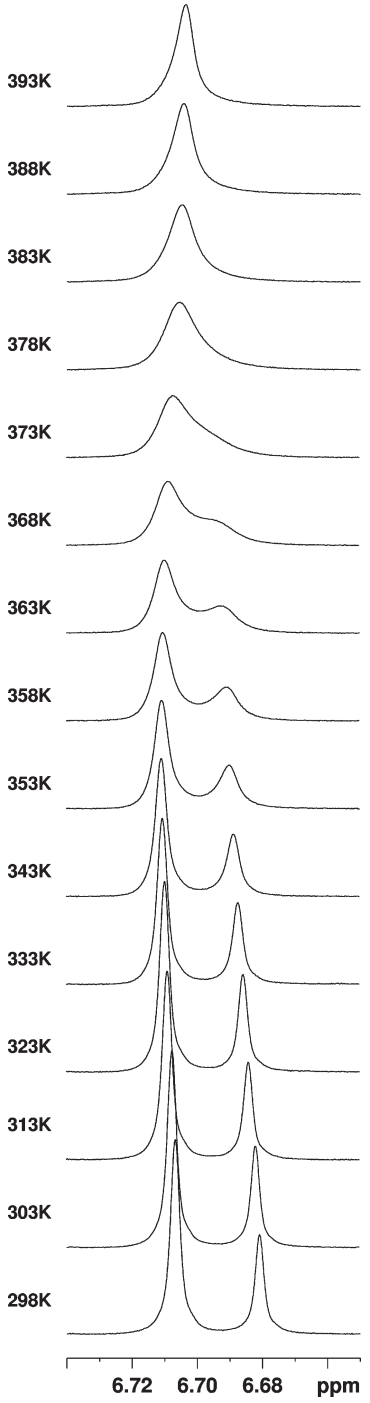


FIGURE 3. Expansion of the aromatic region of the VT-NMR spectra of **10**,**10′c** in DMSO-d_6 at 500 MHz ($\Delta\nu$ = 13 Hz).

at low temperature by HPLC. In fact, a baseline separation of **10c** and **10′c** was attempted by maintaining the temperature of the HPLC column at 4 °C (eluent: 75/25, hexane/EtOAc). At this temperature separation failed, and only one broad peak was obtained on the chromatogram. This result suggested that the equilibration of the rotamers **10c** and **10′c** was too fast at 4 °C (half-lives around 6.7 and 2.4 min) to distinguish them. Consequently, according to our observations and results, the equilibrium should be slow at a lower temperature.

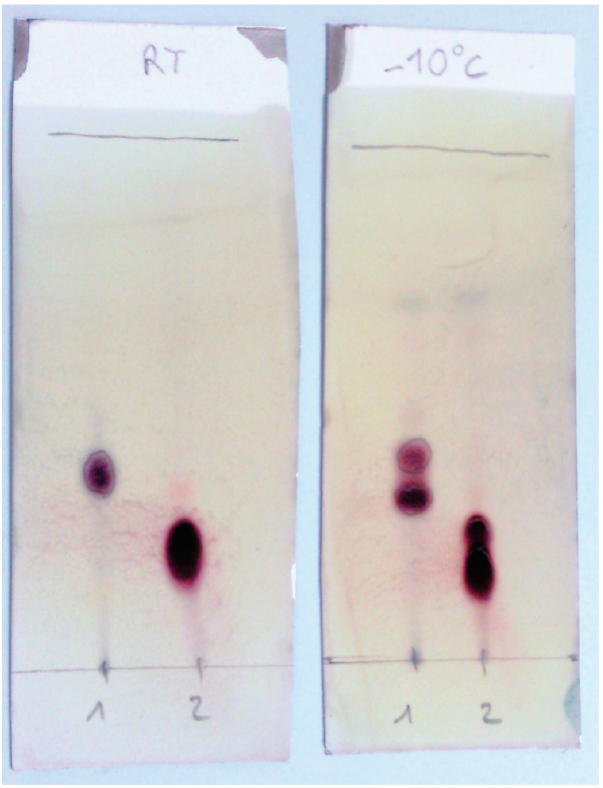


FIGURE 4. TLC plates at rt (left) and −10 °C (right) (eluent: 7:3 hexane/EtOAc) for **10**,**10′b** (1) and **10**,**10′c** (2).

In order to verify this hypothesis, we achieved separation of **10b**,**c** and **10′b**,c by TLC (7:3, hexane/EtOAc) at −10 °C (half-lives of 44.5 and 15.4 min for **10c** and **10′c**, respectively) by placing the plate in the frozen compartment of a refrigerator (Figure 4). Two spots appeared in each case and were identified as **10** and **10′** by UV (at 254 nm) and after staining with vanillin. As a reference, TLC was performed at room temperature with the same eluent, and only one spot was obtained in each case.

To illustrate more explicitly the interconversion, 2D TLCs were then run on rotamers **10**,**10′c** at three different temperatures (Figure 5). At very low temperature (−20 °C), four spots appeared, in which the two most intense spots (right) correspond to the major rotamer **10c** and the two less intense spots (left) to the minor rotamer **10′c**.

These compounds possess four asymmetric centers (C1, C2, C3 and C4), and a fifth element of chirality (namely an axis of chirality along the Car−C3 bond) must be present in order to account for the apparent diastereoisomers seen by NMR at room temperature and by TLC at very low temperature. This point suggests that **10** and **10′** are mixtures of rotational diastereoisomers (Figure 2).

In order to confirm this conclusion we prepared, according to the same synthetic route as for (−)-**1**, the endocyclic epoxide **14** with a symmetrical aromatic moiety from phloroglucinol in three steps (Scheme 4). As expected, epoxide **14** was isolated as a single isomer. Furthermore, in compound **14**, the two *o*-methoxy groups and the two *meta* protons appeared at different chemical shifts in the ^{1}H NMR spectrum (in DMSO-d_6 at 500 MHz). The corresponding signals also showed different chemical shifts in the ^{13}C NMR

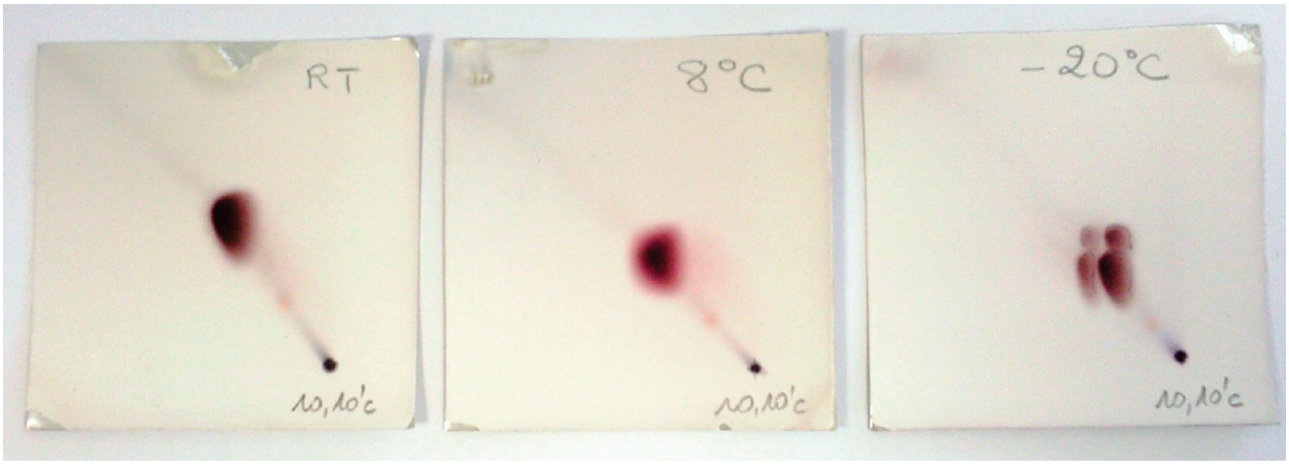
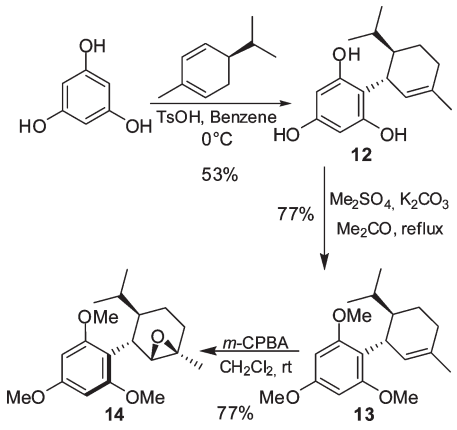


FIGURE 5. 2D TLC plates at rt (left), 8 °C and −20 °C (right) (eluent: 7:3 hexane/EtOAc) for **10**,**10′c**.

SCHEME 4



spectrum (see the Supporting Information). This meant that the rotation of the aryl ring was slow enough on the NMR time scale to make the two *o*-methoxy groups and the two *meta* protons diastereotopic. This rotamer (**14**) was also studied by VT-NMR (Figure 6; see the Supporting Information for all spectra). When rotamer **14** was heated in DMSO-d_6 at 500 MHz, the two doublets with a small *meta* coupling (2.1 Hz) for the diastereotopic aromatic protons broadened and coalesced at about 368 K (with an uncertainty of 5°) and emerged at higher temperature as one sharp singlet. The rate constant k_c for these *meta* coupling protons was about 30 s^{-1} calculated by application of an alternative equation to the Gutowsky−Holm equation[11a,b] (see the Supporting Information for more details) and $\Delta G^{\ddagger} = 80.4 \pm 1.3$ kJ·mol^{-1}. For the *o*-methoxy protons, the coalescence was observed at 358 K (±5°) and we found $k_c = 16.2$ s^{-1}. The value found for $\Delta G^{\ddagger}$ (79.9 ± 1.3 kJ·mol^{-1}) is in good agreement with those obtained from the *meta* protons.

Finally, we also observed this interesting phenomenon with alkenes **9a**−**c** (Scheme 3) where rotation at the Car−C3 bond is restricted but with lower rotation barriers than for epoxides **10** and **10′**. Indeed, in ^{1}H NMR spectra, a very broad signal for the benzylic proton (3-H) and a slightly less-broad signal for the neighboring alkene proton (2-H) were found in compounds **9a**−**c**. In addition, the corresponding signals (C2 and C3) appeared with difficulty in the ^{13}C NMR

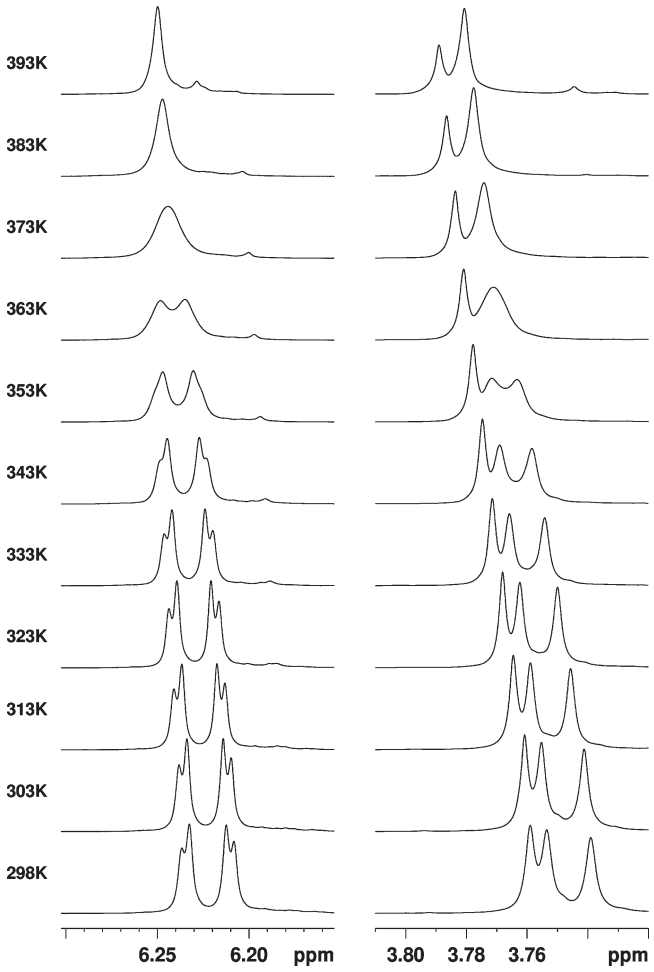
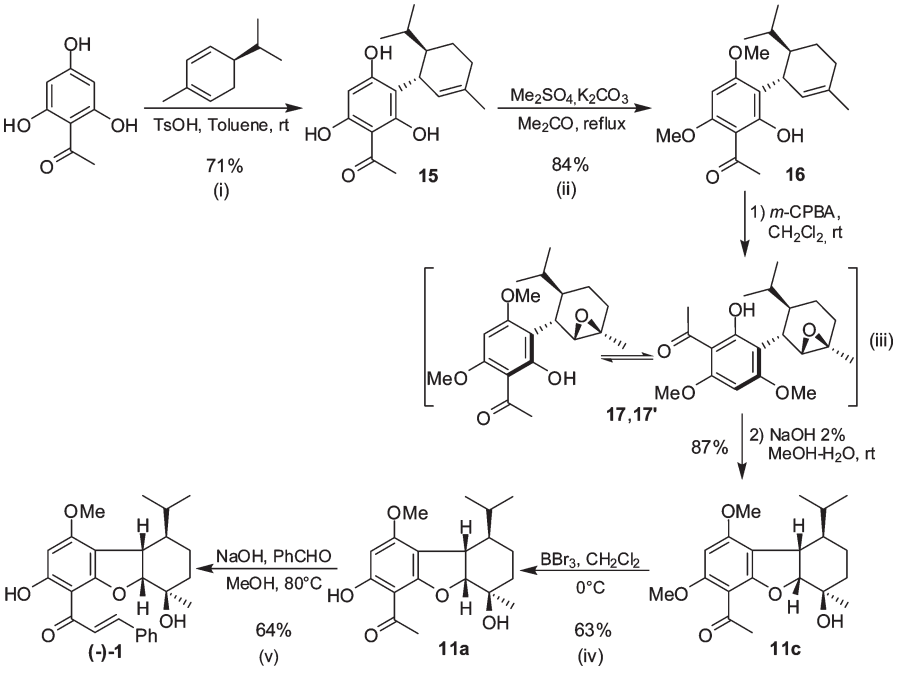


FIGURE 6. Expansion of the aromatic and the methoxy regions of the VT-NMR spectra of **14** in DMSO-d_6 at 500 MHz ($\Delta\nu$ = 12.5 and 7.3 Hz, respectively).

spectra of **9a**−**c** (see the Supporting Information for NMR spectra). These dynamic effects were assigned to a restricted sp^2-sp^3 rotation with a coalescence temperature between 15 and 25 °C.[11b,13a,13c] Variable-temperature (VT) NMR studies were already reported for this type of compounds.[13a,c]

SCHEME 5



As a conclusion, the high rotation barriers (around 80 kJ·mol^{-1}) for rotamers **10**, **10′c**, and **14** could therefore be explained by the rigidity of the endocyclic epoxide and the presence of the *ortho*-substituents on the aromatic ring.

Epoxidation is accordingly completely diastereoselective in term of asymmetric centers. In view of this, we wish to revise the reported[6] "mixture of the two diastereomeric epoxides" which turned out to be a mixture of two rotational diastereoisomers.

The last point that required improvement is the preparation of the starting reagent 2,6-dihydroxy-4-methoxyacetophenone **7** which was obtained with a poor yield (~20%) by *para*-methylation of the commercially available phloroacetophenone, due to the low regioselectivity of the reaction.[9] Considering this fact the overall yield of our described synthesis was only 6% over six steps. After several attempts to optimize the reaction yield, we decided to recast the synthesis by slightly modifying our approach (Scheme 5).

In the first key step, the terpenylation was directly conducted with phloroacetophenone, an easily available commercial reagent (instead of **7**). The obtained monoterpenylated derivative **15** was regioselectively dimethylated (step ii). Then, the asymmetric epoxidation of the dimethyl ether **16** was followed by stereospecific intramolecular epoxide ring-opening with the phenolate anion to give the hexahydrodibenzofuran ring **11c** (step iii). Finally, the acetyl-adjacent methyl ether was regioselectively cleaved, the subsequent introduction of the chalcone chain led to the target natural product (−)-**1** (steps iv and v). We planned an improved synthesis of (−)-**1** according to this route (Scheme 5).

Terpenylation of the phloroacetophenone using (−)-α-phellandrene in the presence of a catalytic amount of TsOH (0.2 equiv) gave the monoterpenylated compound **15** in 71% yield. Surprisingly, phloroacetophenone was more reactive than its corresponding *para*-methylated derivative **7** for which terpenylation required a stoichiometric quantity of TsOH. The monoterpenylated derivative **15** was regioselectively converted into its dimethyl ether **16** in good yield in the presence of dimethyl sulfate and K_2CO_3. Then the dimethyl ether **16** was allowed to react with *m*-chloroperoxybenzoic acid generating a mixture of two rotameric epoxides (**17** and **17′**) which were directly opened (without purification by column chromatography) by phenolate anion under basic conditions leading to the desired hexahydrodibenzofuran derivative **11c** in very good yield (87% for two steps). The selective demethylation of the methoxy group by treatment with BBr_3 afforded the phenol **11a** in 63% yield. Finally the chalcone chain was introduced by aldol condensation in the presence of benzaldehyde under alkaline conditions giving (−)-linderol A with good yield (64%).

Conclusion

We have accomplished a concise and improved enantioselective total synthesis of (−)-linderol A after only five steps and from cheap commercial reagents in 21% overall yield. We have also shown that in the epoxidation step, the reaction is diastereoselective and allows to obtain a mixture of two rotameric diastereoisomers.

Experimental Section

2-Acetyl-4-((1*R*,6*R*)-6-isopropyl-3-methylcyclohex-2-enyl)-5-methoxy-1,3-phenylene Diacetate (9a). Ac_2O (3 mL) was added to a solution of **8** (180 mg, 0.57 mmol) in pyridine (2 mL) at rt under a N_2 atmosphere, and the whole was stirred at 70 °C overnight. The reaction mixture was evaporated under reduced pressure, and then the residue was purified by silica gel column chromatography (8:2 petroleum ether/EtOAc) to give **9a** (210 mg, 91%) as a colorless oil: $[\alpha]^{23}_D$ +14 (*c* 0.44, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (s, 1H), 5.09 (s, 1H), 3.80 (m, 4H), 2.40 (s, 3H), 2.31 (s, 3H), 2.12 (s, 3H), 2.03 (m, 2H), 1.90 (m, 1H), 1.78 (dt, J = 12.9 Hz, J = 2.3 Hz, 1H), 1.63 (s, 3H), 1.36 (m,

2H), 0.86 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4 (C), 169.2 (C), 168.5 (C), 160.1 (C), 147.4 (C), 147.1 (C), 132.9 (C), 124.9 (CH), 124.3 (C), 121.1 (C), 102.6 (CH), 55.9 (CH_3), 42.5 (CH), 36.0 (CH), 30.8 (CH_3), 30.6 (CH_2), 28.0 (CH), 23.4 (CH_3), 22.3 (CH_2), 21.5 (CH_3), 21.1 (CH_3), 20.8 (CH_3), 15.9 (CH_3); MS (EI) m/z (rel intensity) 402 (M^+, 0.1), 359 (52), 317 (99), 290 (22), 248 (100), 233 (30); HRMS (EI) m/z calcd for $C_{23}H_{30}O_6$ 402.2042, found 402.2041.

2-Acetyl-4-((1*R*,6*R*)-6-isopropyl-3-methylcyclohex-2-enyl)-5-methoxy-1,3-phenylene Dibenzoate (9b). BzCl (0.12 mL, 1 mmol) was added to a solution of **8** (123 mg, 0.4 mmol) in pyridine (2 mL) at rt under a N_2 atmosphere, and the whole was stirred at 70 °C overnight. The reaction mixture was evaporated under reduced pressure, and then the residue was purified by silica gel column chromatography (98:2 CH_2Cl_2/ EtOAc) to give **9b** (170 mg, 82%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25−8.06 (m, 4H), 7.87−7.42 (m, 6H), 6.72 (s, 1H), 5.12 (s, 1H), 3.96 (br s, 1H), 3.84 (s, 3H), 2.40 (s, 3H), 2.00−1.00 (m, 9H), 0.89 (d, J = 6.9 Hz, 3H), 0.80 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3 (C), 165.0 (C), 164.5 (C), 160.2 (C), 147.7 (C), 147.3 (C), 134.5 (CH), 134.0 (CH), 133.5 (CH), 133.4 (C), 130.5 (CH), 130.3 (CH), 130.26 (CH), 129.0 (2C), 128.9 (CH), 128.8 (CH), 128.3 (CH), 125.7 (C), 124.8 (C), 124.5 (CH), 102.9 (CH), 56.0 (CH_3), 43.1 (CH), 36.2 (CH), 31.1 (CH_3), 30.3 (CH_2), 28.1 (CH), 23.1 (CH_3), 22.3 (CH_2), 21.7 (CH_3), 16.0 (CH_3); MS (EI) m/z (rel intensity) 526 (M^+, 0.3), 422 (99), 421 (100), 379 (98), 351 (90), 122 (64), 106 (66), 105 (100); HRMS (EI) m/z calcd for $C_{33}H_{34}O_6$ 526.2355, found 526.2337.

2-Acetyl-6-((1*R*,6*R*)-6-isopropyl-3-methylcyclohex-2-enyl)-3,5-dimethoxyphenyl Acetate (9c). Ac_2O (0.75 mL) was added to a solution of **16** (43 mg, 0.13 mmol) in pyridine (0.5 mL) at rt under a N_2 atmosphere, and the whole was stirred at 90 °C overnight. The reaction mixture was evaporated under reduced pressure, and then the residue was purified by silica gel column chromatography (9:1 petroleum ether/EtOAc) to give **9c** (46 mg, 94%) as a colorless oil: ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.66 (s, 1H), 4.93 (s, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.72 (br s, 1H), 2.32 (s, 3H), 2.12−1.63 (m, 7H),1.59 (s, 3H), 1.32 (m, 1H), 1.23 (dq, J = 12.4 Hz, J = 5.2 Hz, 1H), 0.79 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 199.3 (C), 169.0 (C), 160.6 (C), 157.1 (C), 147.1 (C), 132.1 (C), 125.5 (CH), 117.6 (C), 117.0 (C), 94.0 (CH), 56.4 (CH_3), 56.3 (CH_3), 42.4 (CH), 35.4 (CH), 31.7 (CH_3), 30.3 (CH_2), 27.9 (CH), 23.5 (CH_3), 22.4 (CH_2), 21.6 (CH_3), 20.8 (CH_3), 16.2 (CH_3); MS (EI) m/z (rel intensity) 374 (M^+, 2), 331 (76), 262 (100); HRMS (EI) m/z calcd for $C_{22}H_{30}O_5$ 374.2093, found 374.2051.

General Procedure for the Synthesis of Rotameric Epoxides 10,10′a−c. *m*-CPBA (1.2 to 1.5 equiv) was added to a solution of **9a−c** in CH_2Cl_2 at rt under a N_2 atmosphere, and the whole was stirred for 2 h. The reaction mixture was treated with saturated K_2CO_3 and extracted with CH_2Cl_2. The organic layer was washed, dried, and evaporated. The residue was purified by silica gel column chromatography to give rotameric epoxides **10,10′a−c**.

2-Acetyl-4-((1*S*,2*S*,3*R*,6*R*)-3-isopropyl-6-methyl-7-oxabicyclo-[4.1.0]heptan-2-yl)-5-methoxy-1,3-phenylene Diacetate (10,10′a): 90%, dr 72/28; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.62 (s, 0.72H), 6.58 (s, 0.28H), 3.85 (s, 2.16H), 3.84 (s, 0.84H), 3.60 (d, J = 10.7 Hz, 0.28H), 3.06 (d, J = 10.7 Hz, 0.72H), 2.91 (s, 0.28H), 2.80 (s, 0.72H), 2.43 (s, 2.16H), 2.42 (s, 0.84H), 2.33 (s, 0.84H), 2.31 (s, 2.16H), 2.28 (s, 2.16H), 2.26 (s, 0.84H), 2.19−1.99 (m, 1H), 1.82−1.46 (m, 3H), 1.43−1.18 (m, 4H), 0.98−0.68 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5 (C), 198.2 (C), 169.1 (C), 168.7 (C), 168.5 (C), 168.3 (C), 159.8 (C), 159.5 (C), 147.8 (C), 147.6 (C), 147.2 (C), 146.8 (C), 123.0 (C), 122.9 (C), 120.4 (C), 120.2 (C), 103.7 (CH), 102.5 (CH), 64.2 (CH), 64.1 (CH), 58.6 (C), 58.3 (C), 55.9 (CH_3), 55.8 (CH_3), 43.0 (CH), 41.8 (CH), 36.2 (CH), 35.0 (CH), 30.9 (CH_3), 30.8 (CH_3), 30.2 (CH_2), 29.6 (CH_2), 27.9 (CH), 23.0 (CH_3), 22.8 (CH_3), 21.6 (CH_3), 21.4 (CH_3), 21.3 (CH_3), 21.1 (CH_3), 21.08 (CH_3), 20.8 (CH_3), 17.9 (CH_2), 17.4 (CH_2), 15.8 (CH_3), 15.7 (CH_3); MS (EI) m/z (rel intensity 418 (M^+, 0.06), 204 (49), 149 (66), 113 (100); HRMS (EI) m/z calcd for $C_{23}H_{30}O_7$ 418.1992, found 418.1964.

2-Acetyl-4-((1*S*,2*S*,3*R*,6*R*)-3-isopropyl-6-methyl-7-oxabicyclo-[4.1.0]heptan-2-yl)-5-methoxy-1,3-phenylene Dibenzoate (10,10′b): 55%, dr 60/40; TLC (7:3 hexane/EtOAc) at rt R_f 0.36, at −10 °C R_f 0.40 and 0.31; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (m, 4H), 7.67 (m, 2H), 7.52 (m, 4H), 6.79 (s, 0.6H), 6.73 (s, 0.4H), 3.90 (s, 1.8H), 3.88 (s, 1.2H), 3.67 (d, J = 11.6 Hz, 0.4H), 3.13 (d, J = 10.6 Hz, 0.6H), 2.91 (s, 1H), 2.41 (s, 1.8H), 2.39 (s, 1.2H), 2.04−0.69 (m, 13.2H), 0.60 (d, J = 6.8 Hz, 1.8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2 (C), 198.1 (C), 165.2 (C), 164.7 (C), 164.5 (C), 164.4 (C), 160.0 (C), 159.6 (C), 148.1 (C), 147.9 (C), 147.6 (C), 147.2 (C), 134.1 (2CH), 134.0 (2CH), 130.4 (4CH), 130.3 (4CH), 129.1 (2C), 128.84 (2CH), 128.8 (2CH), 128.7 (2CH), 128.66 (2CH), 128.5 (2C), 123.6 (C), 123.5 (C), 121.3 (C), 121.1 (C), 104.1 (CH), 102.9 (CH), 64.25 (CH), 64.22 (CH), 58.7 (C), 58.6 (C), 56.1 (CH_3), 56.0 (CH_3), 43.0 (CH), 41.9 (CH), 36.4 (CH), 35.5 (CH), 31.2 (CH_3), 31.1 (CH_3), 30.3 (CH_2), 29.7 (CH_2), 28.1 (CH), 22.9 (CH_3), 22.5 (CH_3), 21.6 (CH_3), 21.5 (CH_3), 18.0 (CH_2), 17.4 (CH_2), 16.2 (CH_3), 15.8 (CH_3); MS (EI) m/z (rel intensity) 542 (M^+, 1), 350 (66), 315 (36), 105 (100); HRMS (EI) m/z calcd for $C_{33}H_{34}O_7$ 542.2305, found 542.2297.

2-Acetyl-6-((1*S*,2*S*,3*R*,6*R*)-3-isopropyl-6-methyl-7-oxabicyclo-[4.1.0]heptan-2-yl)-3,5-dimethoxyphenyl Acetate (10,10′c): 97%, dr 68/32; TLC (7:3 hexane/EtOAc) at rt R_f 0.22, at −10 °C R_f 0.25 and 0.16; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.39 (s, 0.67H), 6.37 (s, 0.33H), 3.90 (s, 0.99H), 3.89 (s, 2.01H), 3.88 (s, 2.01H), 3.87 (s, 0.99H), 3.53 (d, J = 10.9 Hz, 0.33H), 3.01 (d, J = 10.6 Hz, 0.67H), 2.90 (s, 0.33H), 2.78 (s, 0.67H), 2.48 (s, 2.01H), 2.47 (s, 0.99H), 2.26 (s, 3H), 2.17−1.95 (m, 1H), 1.80−1.10 (m, 7H), 1.01−0.80 (m, 1H), 0.74 (d, J = 6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6 (C), 200.3 (C), 169.4 (C), 169.1 (C), 160.6 (C), 160.2 (C), 157.9 (C), 157.6 (C), 147.8 (C), 147.2 (C), 117.5 (C), 117.3 (C), 116.3 (C), 116.1 (C), 93.2 (CH), 92.1 (CH), 64.7 (CH), 64.6 (CH), 58.6 (C), 58.4 (C), 55.7 (CH_3), 55.6 (CH_3), 42.9 (CH), 42.1 (CH), 35.7 (CH), 34.7 (CH), 31.7 (CH_3), 31.6 (CH_3), 30.8 (CH_2), 30.3 (CH_2), 27.8 (CH), 27.78 (CH), 23.0 (CH_3), 22.8 (CH_3), 21.5 (CH_3), 21.3 (CH_3), 20.9 (CH_3), 20.8 (CH_3), 17.9 (CH_2), 17.4 (CH_2), 15.8 (CH_3), 15.7 (CH_3); MS (EI) m/z (rel intensity) 390 (M^+, 12), 209 (47), 156 (89), 139 (100), 111 (44); HRMS (EI) m/z calcd for $C_{22}H_{30}O_6$ 390.2042, found 390.1986.

General Procedure for the Synthesis of 11a and 11c. The mixture of rotameric epoxides **10,10′a−c** was treated at rt with 2% NaOH solution in MeOH/H_2O (1:1). The solution was stirred at rt for 2 h and then neutralized with 10% HCl. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with water and dried over $MgSO_4$. The solvent was then removed under reduced pressure, and the residue was purified by silica gel column chromatography to give **11a** (from **10,10′a,b**) or **11c** (from **10,10′c**).

1-((5a*R*,6*R*,9*R*,9a*S*)-3,6-Dihydroxy-9-isopropyl-1-methoxy-6-methyl-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*d*]furan-4-yl)ethanone (11a): 76% from **10,10′a** and 86% from **10,10′b**, pale yellow solid; mp 155−158 °C; $[\alpha]^{22}_D$ −84.5 (*c* 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.18 (s, 1H), 6.02 (s, 1H), 4.16 (dd, J = 5.5 and 1.3 Hz, 1H), 3.81 (s, 3H), 3.11 (dd, J = 11.1 and 5.5 Hz, 1H), 2.60 (s, 3H), 1.95−1.60 (m, 3H), 1.55 (br s, 1H), 1.49 (s, 3H), 1.40 (m, 2H), 1.10 (m, 1H), 0.90 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8 (C), 165.0 (C), 162.0 (C), 161.8 (C), 113.1 (C), 102.9 (C), 92.5 (CH), 92.3 (CH), 69.3 (C), 55.4 (CH_3), 46.5 (CH), 39.6 (CH), 35.2 (CH_2), 31.1 (CH_3), 28.2 (CH_3), 27.1 (CH), 21.7 (CH_3), 17.1 (CH_2), 15.4 (CH_3); IR (KBr) 3442, 2958, 2930, 1619, 1362, 1293, 1208, 1149, 1054 cm^{-1}; MS (EI) m/z (rel intensity) 334 (M^+, 28), 249 (100), 207 (30); HRMS (EI) m/z calcd for

$C_{19}H_{26}O_5$ 334.1780, found 334.1779. Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.46; H, 7.68.

1-((5a*R*,6*R*,9*R*,9a*S*)-6-Hydroxy-9-isopropyl-1,3-dimethoxy-6-methyl-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*d*]furan-4-yl)ethanone (11c): 99%, pale yellow solid; mp 53−55 °C; $[\alpha]^{22}_D$ −72.5 (*c* 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1H), 4.10 (d, J = 5.3 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.12 (dd, J = 11.1 and 5.3 Hz, 1H), 2.51 (s, 3H), 1.89 (m, 1H), 1.74 (m, 2H), 1.57 (br s, 1H), 1.46 (s, 3H), 1.41 (m, 2H), 1.11 (m, 1H), 0.90 (d, J = 6.9 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.7 (C), 160.7 (C), 159.8 (C), 158.3 (C), 114.7 (C), 108.8 (C), 91.7 (CH), 88.5 (CH), 69.5 (C), 56.2 (CH_3), 55.3 (CH_3), 46.2 (CH), 39.7 (CH), 35.1 (CH_2), 32.5 (CH_3), 28.1 (CH_3), 27.1 (CH), 21.7 (CH_3), 17.2 (CH_2), 15.4 (CH_3); IR (KBr) 3432, 2958, 2920, 2849, 1605, 1459, 1262, 1102 cm^{-1}; MS (EI) m/z (rel intensity) 348 (M^+, 38), 263 (68), 222 (50), 221 (100), 205 (36), 149 (36); HRMS (EI) m/z calcd for $C_{20}H_{28}O_5$ 348.1937, found 348.1937.

2-((1*R*,6*R*)-6-Isopropyl-3-methylcyclohex-2-enyl)benzene-1,3,5-triol (12). A solution of phloroglucinol dihydrate (250 mg, 1.54 mmol) in CH_3CN/benzene (5 mL/5 mL) was added dropwise to a suspension of (−)-α-phellandrene (0.7 mL, 420 mg, 4.34 mmol) and dried TsOH (90 mg, 0.47 mmol) in dry benzene under ice cooling and a N_2 atmosphere. The whole was stirred for 2 h. After neutralization with saturated $NaHCO_3$, the mixture was extracted with EtOAc. The combined extracts were washed, dried, and evaporated. The residue was chromatographed (95:5 CH_2Cl_2/ EtOAc) to give **12** (214 mg, 53%): $[\alpha]^{25}_D$ +35.9 (*c* 1.31, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 5.81 (s, 2H), 5.28 (s, 1H), 3.73 (br d, J = 9.0 Hz, 1H), 2.20−1.94 (m, 2H), 1.88 (m, 1H), 1.75 (m, 1H), 1.68 (s, 3H), 1.56 (m, 1H), 1.32 (m, 1H), 0.82 (m, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 158.4 (C), 157.2 (C), 135.6 (C), 127.9 (CH), 110.3 (2C), 95.9 (2CH), 44.0 (CH), 36.7 (CH), 31.9 (CH_2), 29.2 (CH), 24.0 (CH_2), 23.7 (CH_3), 22.0 (CH_3), 16.8 (CH_3); IR (KBr) 3432, 2949, 2930, 2863, 1619, 1456, 1225, 1137 cm^{-1}; MS (EI) m/z (rel intensity) 262 (M^+, 46), 192 (87), 177 (100); HRMS (EI) m/z calcd for $C_{16}H_{22}O_3$ 262.1569, found 262.1568.

2-((1*R*,6*R*)-6-Isopropyl-3-methylcyclohex-2-enyl)-1,3,5-trimethoxybenzene (13). A suspension of **12** (107 mg, 0.41 mmol), Me_2SO_4 (0.15 mL, 206 mg, 1.63 mmol), and anhydrous K_2CO_3 (198 mg, 1.43 mmol) in Me_2CO (5 mL) was stirred under reflux for 6 h. The reaction mixture was filtered and evaporated under reduced pressure to give a residue that was purified by silica gel column chromatography (70:30 petroleum ether/CH_2Cl_2) to yield **13** (96 mg, 77%) as a colorless oil: $[\alpha]^{25}_D$ +125.9 (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 2H), 5.12 (s, 1H), 3.80 (m, 4H), 3.72 (s, 6H), 2.20−1.89 (m, 3H), 1.72 (m, 1H), 1.64 (s, 3H), 1.49−1.23 (m, 2H), 0.80 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8 (C), 159.1 (C), 131.4 (C), 126.4 (CH), 114.8 (2C), 91.5 (2CH), 55.9 (2CH_3), 55.1 (CH_3), 42.1 (CH), 35.6 (CH), 31.0 (CH_2), 28.4 (CH), 23.4 (CH_3), 23.1 (CH_2), 21.6 (CH_3), 16.1 (CH_3); IR (NaCl) 2949, 2930, 2830, 1603, 1589, 1463, 1452, 1220, 1201, 1154, 1118 cm^{-1}; MS (EI) m/z (rel intensity) 304 (M^+, 24), 234 (100), 203 (57); HRMS (EI) m/z calcd for $C_{19}H_{28}O_3$ 304.2038, found 304.2042.

(1*R*,4*R*,5*S*,6*S*)-4-Isopropyl-1-methyl-5-(2,4,6-trimethoxyphenyl)-oxabicyclo[4.1.0]heptane (14). *m*-CPBA (105 mg, 0.61 mmol) was added to a solution of **13** (140 mg, 0.46 mmol) in CH_2Cl_2 (5 mL) at rt under a N_2 atmosphere, and the whole was stirred for 1.5 h. The reaction mixture was treated with saturated K_2CO_3, extracted with CH_2Cl_2. The organic layer was washed, dried, and evaporated. The residue was chromatographed (70:30 petroleum ether/EtOAc) to give **14** (113 mg, 77%) as a colorless oil: $[\alpha]^{25}_D$ +34.2 (*c* 0.91, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.44 (d, J = 10.8 Hz, 1H), 2.82 (s, 1H), 2.04 (dt, J = 13.9 and 3.2 Hz, 1H), 1.73 (m, 1H), 1.51−1.12 (m, 7H), 0.77 (d, J = 6.9 Hz, 3H), 0.73 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5 (C), 159.0 (C), 158.8 (C), 112.9 (C), 91.0 (CH), 90.2 (CH), 66.1 (CH), 58.7 (C), 55.5 (CH_3), 55.3 (CH_3), 55.1 (CH_3), 42.8 (CH), 34.0 (CH), 30.7 (CH_2), 28.0 (CH), 23.1 (CH_3), 21.5 (CH_3), 17.9 (CH_2), 15.9 (CH_3); IR (NaCl) 2944, 2840, 1605, 1586, 1456, 1418, 1220, 1201, 1187, 1149, 1123, 1106, 1038 cm^{-1}; MS (EI) m/z (rel intensity) 320 (M^+, 51), 302 (32), 300 (30), 259 (77), 181 (100), 168 (92); HRMS (EI) m/z calcd for $C_{19}H_{28}O_4$ 320.1988, found 320.1990. Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 70.86; H, 8.58.

1-(2,4,6-Trihydroxy-3-((1*R*,6*R*)-6-isopropyl-3-methylcyclohex-2-enyl)phenyl)ethanone (15). A solution of 2′,4′,6′-trihydroxyacetophenone monohydrate (500 mg, 2.69 mmol) in toluene/CH_3CN (5 mL/10 mL) was added dropwise to a suspension of (−)-α-phellandrene (1 mL, 879 mg, 6.45 mmol) and TsOH (110 mg, 0.58 mmol) in dry toluene (23 mL) at rt under a N_2 atmosphere. The whole was stirred for 1 h. After neutralization with saturated $NaHCO_3$, the mixture was extracted with EtOAc. The combined extracts were washed, dried, and evaporated. The residue was chromatographed (96:4 CH_2Cl_2/ EtOAc) to give **15** (583 mg, 71%) as a pale yellow solid: mp 69−71 °C; $[\alpha]^{23}_D$ +11.6 (*c* 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 5.84 (s, 1H), 5.17 (s, 1H), 3.76 (br d, J = 9.1 Hz, 1H), 2.60 (s, 3H), 2.18−1.90 (m, 3H), 1.71 (m, 1H), 1.62 (s, 3H), 1.50 (m, 1H), 1.30 (m, 1H), 0.82 (d, J = 7.0 Hz, 3H), 0.79 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6 (C), 165.5 (C), 164.8 (C), 162.1 (C), 134.3 (C), 127.4 (CH), 110.3 (C), 105.5 (C), 95.2 (CH), 43.0 (CH), 36.4 (CH), 33.0 (CH_3), 31.9 (CH_2), 29.5 (CH), 24.1 (CH_2), 23.7 (CH_3), 22.0 (CH_3), 16.9 (CH_3); IR (KBr) 3413, 2953, 2925, 2863, 1617, 1440, 1362, 1295, 1269, 1246 cm^{-1}; MS (EI) m/z (rel intensity) 304 (M^+, 23), 234 (35), 219 (100), 181 (24), 153 (25); HRMS (EI) m/z calcd for $C_{18}H_{24}O_4$ 304.1675, found 304.1675. Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 70.93; H, 7.85.

1-(2-Hydroxy-3-((1*R*,6*R*)-6-isopropyl-3-methylcyclohex-2-enyl)-4,6-dimethoxyphenyl)ethanone (16). A suspension of **15** (619 mg, 2.04 mmol), Me_2SO_4 (641 mg, 5.09 mmol), and anhydrous K_2CO_3 (560 mg, 4.06 mmol) in Me_2CO (20 mL) was stirred under reflux for 4 h. The reaction mixture was filtered and evaporated under reduced pressure to give a residue that was purified by column chromatography (98:2 petroleum ether/EtOAc) to yield **16** (588 mg, 87%) as a pale yellow solid: mp 76−79 °C; $[\alpha]^{25}_D$ +126.1 (*c* 1.06, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.91 (s, 1H), 5.87 (s, 1H), 5.10 (s, 1H), 3.90−3.64 (m, 7H), 2.53 (s, 3H), 2.15−1.80 (m, 3H), 1.68 (m, 1H), 1.59 (s, 3H), 1.29 (m, 2H), 0.75 (d, J = 6.9 Hz, 3H), 0.70 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4 (C), 164.7 (C), 164.3 (C), 161.7 (C), 132.0 (C), 125.9 (CH), 112.7 (C), 105.9 (C), 86.0 (CH), 55.4 (CH_3), 55.2 (CH_3), 41.3 (CH), 35.3 (CH), 33.2 (CH_3), 30.7 (CH_2), 28.5 (CH), 23.4 (CH_3), 22.5 (CH_2), 21.6 (CH_3), 16.2 (CH_3); IR (KBr) 3437, 2949, 2920, 2365, 1615, 1418, 1274, 1217, 1118, 1092 cm^{-1}; MS (EI) m/z (rel intensity) 332 (M^+, 26), 262 (100), 247 (70); HRMS (EI) m/z calcd for $C_{20}H_{28}O_4$ 332.1988, found 332.1992. Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.35; H, 8.54.

11c. *m*-CPBA (295 mg, 1.72 mmol) was added to a solution of **16** (457 mg, 1.38 mmol) in CH_2Cl_2 (17 mL) at rt under a N_2 atmosphere, and the whole was stirred for 1 h. NaOH (2% in MeOH−H_2O 1:1, 17 mL) was added to the reaction mixture. The solution was stirred at rt for 30 min and then neutralized with 10% HCl. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with H_2O and dried over $MgSO_4$. The solvent was then removed under reduced pressure, and the residue was purified by silica gel column chromatography (6:4 petroleum ether/EtOAc) to give **11c** (420 mg, 87%) as a pale yellow solid.

11a. BBr_3 (1 M in CH_2Cl_2, 1.2 mL, 1.2 mmol) was added dropwise to a solution of **11c** (280 mg, 0.8 mmol) in CH_2Cl_2 (5 mL) under ice cooling and a N_2 atmosphere. The whole was stirred for 10 min at 0 °C. After the addition of H_2O, the reaction mixture was stirred for 30 min at rt and then extracted with CH_2Cl_2. The combined extracts were washed, dried, and evaporated.

The residue was chromatographed (75:25 petroleum ether/EtOAc) to give **11a** (168 mg, 63%) as a pale yellow solid.

(*E*)-1-((5a*R*,6*R*,9*R*,9a*S*)-3,6-Dihydroxy-9-isopropyl-1-methoxy-6-methyl-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*d*]furan-4-yl)-3-phenylprop-2-en-1-one ((−)-1). NaOH (56 mg, 1.4 mmol) and benzaldehyde (60 mg, 0.57 mmol) was added to a solution of **11a** (95 mg, 0.28 mmol) in MeOH (4 mL) at rt under a N_2 atmosphere. The mixture was stirred for 3 h at 80 °C, neutralized with HCl (1 N), and extracted with CH_2Cl_2. The combined extracts were washed, dried, and evaporated. The residue was chromatographed (98:2 CH_2Cl_2/ EtOAc) to give (−)-**1** (76 mg, 64%) as a yellow powder: mp 179−181 °C; $[\alpha]^{22}_D$ −35.6 (*c* 0.88, $CHCl_3$); $[\alpha]^{26}_D$ −25.9 (*c* 0.68, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.96 (s, 1H), 8.09 (d, J = 15.6 Hz, 1H), 7.86 (d, J = 15.6 Hz, 1H), 7.61 (m, 2H), 7.39 (m, 3H), 6.09 (s, 1H), 4.24 (dd, J = 5.4 and 0.9 Hz, 1H), 3.83 (s, 3H), 3.13 (dd, J = 11.1 and 5.5 Hz, 1H), 1.81 (m, 3H), 1.62 (s, 3H), 1.45 (m, 3H), 1.12 (m, 1H), 0.90 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0 (C), 166.7 (C), 162.1 (C), 161.5 (C), 143.4 (CH), 135.3 (C), 130.3 (CH), 128.9 (2CH), 128.4 (2CH), 125.8 (CH), 113.3 (C), 103.3 (C), 93.0 (CH), 92.3 (CH), 69.3 (C), 55.4 (CH_3), 46.5 (CH), 39.5 (CH), 35.4 (CH_2), 28.3 (CH), 27.1 (CH_3), 21.7 (CH_3), 17.2 (CH_2), 15.4 (CH_3); IR (KBr) 3449, 2953, 1631, 1586, 1345, 1236, 1206, 1142 cm^{-1}; MS (EI) m/z (rel intensity) 422 (M^+, 47), 337 (100), 295 (26); HRMS (EI) m/z calcd for $C_{26}H_{30}O_5$ 422.2093, found 422.2103.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **9a**−**c**, mixtures of **10**,**10′a**−**c**, **11a**−**c**, **12**−**16**, and (−)-**1** and VT ^{1}H NMR spectra of **10**,**10′c** and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.